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DEPARTMENT OF THE ARMY  
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STUDY OF THE MESENTERIC CIRCULATION  
IN ANIMALS TREATED WITH A BACTERIAL ENDOTOXIN

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Report Presented During the 28 May 1947 Session by Mr. Gaston Ramon

We wanted to add to our knowledge on the way in which endotoxins act (see our two communications which were presented to the Microbiology Society in January 1947; they will be published in les Annales de l'Institut Pasteur (Pasteur Institute Yearbook)); we therefore made a direct examination of the mesentery in an effort to study the vascular reactions and the circulation in the animals treated with strong doses of typhus endotoxin. The method we used recalls the method used recently by R. Chambers and B. W. Zweifach (Am. J. Anat., 75, 1944, page 173); we can recommend this method because of its simplicity.

Our experiments involved mice (20 g) and guinea pigs (250 g) of both sexes, in perfect physiological condition. The animals were anesthetized either by means of ether (mice), administered by way of inhalation, or by means of ethyleurethane (guinea pigs) in the form of a subcutaneous injection. Whenever the anesthesia which we obtained was satisfactory, the abdomen of these animals was shaved; then, by means of a narrow opening made by means of a pair of scissors in one of the sides of the animal, we very delicately withdrew /extracted/ a loop of the small intestine. This was then placed on a small wooden plate with a perforation in its center so that the loop itself was arranged along the edges of the plate while the mesentery was stretched over the opening. Finally we put this preparation on the stage of a microscope so that the light rays had to go through the mesentery before reaching the objective. Under these conditions, the mesenteric vessels (arteries, arterioles, veins and small veins, as well as capillaries), as well as the cells which they contained (especially leucocytes) could be distinguished clearly. We can

also get a rough idea of the speed of the circulatory current in this fashion. With a little bit of practice, this operation is not at all difficult to perform. However, to make it successful, we must take a certain number of precautions: (a) We must handle the intestine with great delicacy so as to avoid hemorrhages and so as not to tear the mesentery; (b) We must prevent the animal from being chilled (we often performed our experiments in a steam room at a temperature of  $30^{\circ}$  /C/); (c) We must avoid the desiccation of the intestine and the mesentery, something we can easily achieve by placing several drops of Ringer solution on the preparation, from time to time. If we work under these optimum conditions, the microscopic examination of the mesentery can, without any trouble, last 1 hour or even several hours. When we work with normal animals, circulation is suitably performed, without the vessels becoming the seat of any abnormal modifications. On the other hand, in intoxicated animals, we can register a certain number of disorders.

We obtained particularly clear results in guinea pigs. The animals were placed on the stage of the microscope and their mesentery was spread out under the objective; we then injected, into the saphena, a lethal dose of typhic endotoxin which turned out to be deadly within a few hours. At the very moment of the injection, mesenteric circulation did not appear to be disturbed but this circulation speeds up rapidly after a few minutes and the speed up often is quite considerable. At the same time, contractions appeared along the medium-calibre arteries and the arterioles; the amplitude of these contractions varies -- it is not rare for it to be very great -- and the contractions reach a more or less large segment of the vessel. These contractions occur also, but less violently, on the level of the veins. As far as the capillaries are concerned, their walls do not seem to undergo any change. The contractions continue for a certain time and then, without any apparent reason, they yield to a vasodilatation which is generally accompanied by a slowdown in the current /flow/. Sometimes this dilatation becomes quite considerable. The circulation slows down rather extremely and it might even stop. But it resumes abruptly after a few minutes, when a new wave of contractions manifests itself. The leucocytes roll along the vascular walls and on the level of the red blood corpuscles more or less rapidly, as a function of the speed of the flow. This series of phenomena keeps repeating itself under the same conditions, while the intoxication progresses. In the terminal phase of the intoxication, however, the vascular contractions are less clear and in the end, we get a generalized and lasting vasodilatation. Circulation slows down. It eventually stops shortly before the animal's death.

We observed roughly the same thing in our mice (injection of bacterial poison into one of the caudal veins); but in these animals the intoxication progresses somewhat more slowly and this excessively prolongs the examination; we thought that the vascular reactions were less easy to follow here.

The results which we have just reported seem to us to be interesting for several reasons.

a. The vasoconstriction phenomena, which we observed, recall those

which were pointed out by various other authors (J. H. Page and R. G. Abell, J. of exp. Med., 77, 1943, p. 216; B. W. Zweifach and colleagues., Am. J. of Physiol., 142, 1944, p. 80) in the course of studies on traumatic shock. In this new analogy, we find supplementary proof in favor of the idea which we advanced (see above: Two communications presented to the Microbiology Society in January 1947), in other words, the state of intoxication brought about by a bacterial endotoxin is rather like the state of traumatic shock.

b. On the other hand, the fact that the mesenteric circulation, although disturbed, continues nevertheless until the animal's death, in other words, the fact that there is really no blood stasis in the mesentery, tells us that the inhibition of the diapedesis (Comptes rendus [Transactions], 222, 1946, p. 699; 223, 1946, p. 1037) is not simply caused by an entirely defective blood irrigation.

The Academy met in secret committee [session] at 1540.

The session ended at 1615.